

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Rainer Zimmermann, et al.  
Serial No. : 08/619,280  
Filed : March 18, 1996  
For : ISOLATED DIMERIC FIBROBLAST  
ACTIVATION PROTEIN ALPHA, AND  
USES THEREOF  
Art Unit : 1818  
Examiner : M. Allen

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Hon. Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

DECLARATION

Norman D. Hanson hereby declares as follows:

1. I am the attorney in charge of the subject application, and its parent application, Serial No. 08/230,491, filed April 20, 1994.

2. The parent application is incorporated by reference at page 2, lines 1-4 of the current application.

3. In the course of prosecution of the parent application, I submitted an amendment on November 13, 1995. This amendment

included sequence information. This amendment was received and entered in the parent application

4. When the subject continuation-in-part application was filed, I submitted a proper request, under 37 C.F.R. § 1.821(e) to have sequence information transferred from the parent application. I properly referred to the date of the sequence submission, and I properly included a paper copy of the material. I also expressly stated that no new matter was presented.

5. It is not clear to me why this declaration was not acceptable. There is no reason for this on the record.

6. Nonetheless, I hereby state that the material submitted on March 18, 1996 is identical to material submitted in the parent application on November 13, 1995. The paper copy submitted on March 18, 1996 was prepared from the same computer readable form of sequence information sent to the USPTO on November 13, 1995. I compared the paper copy submitted on November 15, 1995 to that submitted on March 18, 1996 and, to the best of my knowledge, these are identical, and no new matter is presented.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the

like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

August 20, 1997

Date

A handwritten signature in dark ink, appearing to read 'Norman D. Hanson', written over a horizontal line.

Norman D. Hanson  
Reg. No. 30,946

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Wolfgang J. Rettig, et al.  
 Serial No. : 08/230,491  
 Filed : April 20, 1994  
 For : ISOLATED NUCLEIC ACID MOLECULE  
 CODING FOR FIBROBLAST ACTIVATION  
 PROTEIN ALPHA AND USES THEREOF  
 Art Unit : 1812  
 Examiner : M. Allen

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 Hon. Commissioner of Patents  
 and Trademarks  
 Washington, D.C. 20231

DECLARATION

The undersigned hereby declare as follows:

1. We are the inventors of the invention described and claimed in the above-referenced patent application. We are fully familiar with its content.
2. We wish to bring the Examiner's attention to errors in the nucleotide sequence and the amino acid sequence of this application.

3. Specifically, three nucleotides need to be added, as follows:

With reference to SEQ ID NO: 1, a G has to be added between bases 2084-2085, 2085-2086, and 2216-2217. This results in a need to change amino acids 626-668 in figure 3. For convenience, copies of original figure 3 and replacement figure 3 are attached, with pertinent material boxed.

4. We became aware of this error after we had isolated and sequenced the murine FAP $\alpha$  gene. We found a very high degree of homology with the human sequence (over 95%), except for the stretch corresponding to amino acids 626-668.
5. As a result, we resequenced the clone described in the application, i.e., pFAP 38, using the methodologies described in this application. It was at this point that we found the omitted bases.
6. We would note that the sequencing was carried out using Sanger et al., Proc. Natl. Acad. Sci. USA 74: 5463-5467 (1979), noted at page 11 of the patent application. It is well known that the Sanger methodology sometimes does not identify adjacent "Gs" in a nucleotide sequence, and "reads" 2 G moieties as a single moiety. Exemplary are the attached materials, i.e., Sambrook & Maniatis, Molecular Cloning, A Laboratory Manual

(CSH, 1989), p. 13.10; Mizusawa, et al., Nucl. Acids Res. 14(3): 1319-1324 (1986); Seela, U.S. Patent No. 4,804,748 (February 14, 1989). That is indeed what happened here.

7. The error in the sequences was inadvertent, and no deceptive intent is involved. Any inconvenience to the PTO is regretted.
8. As a result of the need to correct the sequences, additional materials in the application must be changed at page 12, lines 8, 9, 12, 13, 22, 23 and page 13, lines 7 and 8.
9. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may

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jeopardize the validity of the application or any patent  
issued thereon.

7/27/95

Date

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Date

7/27/95

Date

Wolfgang Pottig  
Wolfgang PottigMatthew Scanlan  
Matthew ScanlanPilar Gafin-Chessa  
Pilar Gafin-Chessa

FAP	1	MKTWVXV J*ATSAVLALLVMCIVLRPSRVH E. IMRALTLKDILN	49
CD26	1	---PW---LL-LLGAA-LVTIITVPV--LNKGTDDATADSRKTY--T-Y-K	50
FAP	50	GTFSYKTFPPNWISGQEYLHQSA DNNIVLYNIETGQSYTILSNRTMKSV*	98
CD26	51	N-YRL-LYSLR---DH---YKQ*E---LVF-A-Y-N-SVF-E-S-FDEFG	99
FAP	99	*NASNYGLSPDRQFVYLES DYSKLRYSYTATYIIYDLNNGEFVRGNELP	147
CD26	100	HSIND-SI---G--IL--YN-V-Q--H-----S-D-----NKRQLITEERI-	149
		<u>fap-1</u>	
FAP	148	RPIQYLWSPVGS KLAYVYQNNIYLKQRP GPPFQITFNGRENKIFNGIP	197
CD26	150	NNT-WVT-----H-----WN-D--V-IE-NL-SYR--WT-K-DI-Y---T	199
		<u>fap-2</u>	
FAP	198	DWVYEEMLP TKYALWSPNGKFLAYAEFNDKDIPVIAYSYYGDE**QYP	245
CD26	200	-----VFSAYS-----T-----Q---TEV-L-E--F-S--SL---	249
FAP	246	RTINIPYPKAGAKNPVVRIFIIDT***TYPAYVGPQEVFPVAMIASSDYY	292
CD26	250	K-VRV-----V--T-KF-VVN-DSLSSVTNATSIQITA--SMLIG-H-	299
FAP	293	FSWLTWVTDERVCLQWLKRVQNVSVLSICDFREDWQTDWDCPKTQEHIEES	342
CD26	300	LCDV--A-Q--IS-----R-I--Y--MD---YD-SSGR-N-LVARQ---M-	349
FAP	343	RTGWAGGFFVSRPVFSYDAISYYKIFSDKDGXKHIHYIKDTVENAIQITS	392
CD26	350	T---V-R-RP-E-H-TL-GN-F---I-NEE--R--C-FQIDKKDCTF--K	399
FAP	393	GKWEAINIFRVTQDSL FYSSNEFE EYPGRRN IYRISIGSYPPSKKCVTCH	442
CD26	400	-T--V-G-EAL-S-Y-Y-I---YKGM--G--L-K-QLSD-T*KVT-LS-E	448
FAP	443	LRKERCQYYTASFSDYAKYYALVCYGPCIPISTLHDGR TDQEIKILEENK	492
CD26	449	-NP-----SV---KE-----Q-R-S---L-LY---SSVN-KGLRV--D-S	498
		<u>fap-3</u>	
FAP	493	ELENALKNIQLPKEEIKKLEVDEITLWYKMI LPPQFDRSKKYPLLIQVYG	542
CD26	499	A-DKM-Q-V-M-SKKLDFIILN-TKF--Q-----H--K-----LD--A	548
FAP	543	GPCSQSVRSVFAVNWISY LASKEGHVIALVDGRGTAFQGD KLLYAVYRKL	592
CD26	549	-----KADT--RL--AT----T-NIIV-SF-----SGY-----IMH-IN-R-	598
FAP	593	GVYEVEDQITAVRKFIEMGFIDEKRIAIWGSY EIRFITGPCIWNHSFQM	642
CD26	599	-TF-----E-A-Q-SK---V-N-----GGYVTSMVLGSGSGVFK	648
FAP	643	WYSSGSS LQGLRVCLHRE*IHGSPNKDDNLEHYKNSTVMARAEYFRNV	691
CD26	649	CGIAPVSRWEY YDSVYT-RYM-L-TPE---D--R-----S---N-KQ-	698
FAP	692	DYLLIHGTADDNVHFQNSAQIAKALVNAQVDFQAMWYSDQNHGLSGLSTN	741
CD26	699	E-----Q-----S-----DVG-----T-ED--IASSTAH	748
FAP	742	*HLYTHMTHFLKQCFSLS D	
CD26	749	Q-I---S--I-----P	

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produced by use of  $^{32}\text{S}$ , there is little loss of resolution between the gel and the autoradiograph. This allows unambiguous determination of several hundred nucleotides of DNA sequence from a single reaction set. Furthermore, the lower energy of  $^{32}\text{S}$  produces less radiolysis, allowing sequencing reactions to be stored for up to 1 week at  $-20^\circ\text{C}$  without noticeable loss of resolution. Thus, if technical problems arise with a polyacrylamide gel, the sequencing reactions can simply be reanalyzed.

#### ANALOGS OF dNTPs

Regions of DNA with dyad symmetry (especially those with a high G + C content) can form intrastrand secondary structures that are not fully denatured during electrophoresis. This can cause an anomalous pattern of migration in which adjacent bands of DNA become compressed to the point where they are difficult to read. Compression is entirely dependent on the presence of secondary structures in DNA and cannot be alleviated by changing the type of DNA polymerase used in the sequencing reaction. However, compressed regions of gels can usually be resolved by using a nucleotide analog such as dITP (2'-deoxyinosine-5'-triphosphate) or 7-deaza-dGTP (7-deaza-2'-deoxyguanosine-5'-triphosphate). These analogs pair weakly with conventional bases and are good substrates for DNA polymerases such as the Sequenase and *Taq* DNA polymerase (Gough and Murray 1983; Mizusawa et al. 1986; Innis et al. 1988). Some compressions are not resolved by 7-deaza-dGTP, others (particularly those occurring in GC-rich regions) are not resolved by dITP. If it is necessary to use analogs, try dITP first (see pages 13.74-13.75). This analog, in contrast to 7-deaza-dGTP, does not affect the sharpness of the DNA bands in the sequencing gel. Any compression that is not resolved by either dITP or 7-deaza-dGTP can almost always be cleared up by determining the sequence of both strands of the DNA.

As discussed above, both forms of Sequenase and *Taq* DNA polymerase tolerate nucleotide analogs better than does the Klenow fragment of *E. coli* DNA polymerase I. In addition, the manufacturer claims that Sequenase version 2.0 is superior to the original enzyme when sequencing templates with strong secondary structure. Version 2.0 is more processive than Sequenase, having less tendency to pause, thereby eliminating "ghost" bands. Furthermore, version 2.0 appears to tolerate nucleotide analogs such as dITP better than does the original version.

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#### 13.10 DNA Sequencing

From : Molecular Cloning 1989  
Maniatis